REMARKS

The Official Action alleges that five references, submitted in the Information Disclosure Statement (IDS) on June 6, 2008, are not in English and no translations are provided. As such, these references were not considered. The five references are listed as reference No. 8 to No. 12, respectively, in the IDS submitted on June 6, 2008.

In response, applicants submit an English translation of the Abstract for reference Nos. 8 and 9; and English translation of reference No. 10. With respect to reference Nos. 11 and 12, applicants submit copies of the same where English translation of the abstract is self-enclosed, for example, see page 824 of reference No. 11 and page 614 of reference No. 12. As such, consideration of the five references is respectfully requested.

Furthermore, in the Official Action, Claims 13, 21 and 27 stand rejected, under 35 U.S.C. §112, 1st paragraph, as allegedly failing to comply with the written description requirement. Specifically, the Official Action alleges that there is no written description for the scope of radical R_2 recited in Claims 13, 21 and 27.

In the response submitted on May 23, 2008, applicants submitted that with respect to the scope of radical R_2, Scheme III on page 17 describes the synthesis of compounds wherein the group –NH-R_2 is connected to the *ortho* position of the N of the pyrazole ring. Specifically, the group –NH-R_2 is introduced via a key reaction wherein intermediate 18 is treated by LiHMDS to form an anion, followed by the treatment of substituted isothiocyanate (R_2-NCS), and then cyclized with hydrazine. See page 17, lines 12-18. Moreover, the specification provides concrete examples to illustrate the above-mentioned Scheme III. See page 34, line 15 to page 36, line 16. Since the above-described key reaction is well recognized in the art of chemistry, and there are many commercially available isothiocyanate reagents with different R_2

substituents, a person skilled in the art would readily understand that applicants had possession of the scope of R_2 as claimed in the present invention. In this regard, applicants enclose (as Exhibit A) a list of 363 commercial available isothiocyanate reagents with different R_2 substituents. Those isothiocyanate reagents are available on the market from known suppliers, such as Aldrich, for example.

In response to the above-described remarks, the Official Action contends that such list of commercial available isothiocyanate reagents does not provide the corresponding source, reference or vendor for the reagents. Therefore, the Examiner concludes that while some of the reagents may be commercially available, the list is not persuasive as to the availability of all reagents listed therein.

In response, applicants enclose (as Exhibit A) a list of 673 commercial available isothiocyanate reagents with different R_2 substituents where the corresponding chemical structure, CAS No. (the standard identification in the chemical field), chemical name, vendor name, and catalog No. Referred to by the vendor for each isothiocyanate reagent are provided. For many of the isothiocyanate reagents, multiple vendors and the corresponding catalog No. Referred to by the vendors are provided. Therefore, applicants submit that above-mentioned list is persuasive as to the commercial availability of all reagents listed therein.

Furthermore, in view of applicants' remarks on May 23, 2008 that variable R_2 has sufficient support because the scheme on page 17 of the specification teaches a generic method of making the claimed products with commercially available isothiocyanates, the Official Action alleges that scheme III (see page 17) would pose numerous problems in utilizing the cited compounds because of the subsequent steps. Specifically, the Official Action contends that March's Advanced Organic Chemistry, 5th ed., 2001 ("March") on pages 1192-1193 teaches that

hydrazine can react with ketones and aldehydes to produce unwanted products rather than the ring formation desired. Furthermore, the Examiner contends that the aminolysis step would cause unwanted side reactions depending upon the R_2-NCS used.

In response, applicants respectfully submit that the Examiner's position regarding the evaluation of the reaction scheme III of the present invention, is incorrect.

Specifically, with respect to the allegation that hydrazine would react with ketones and/or aldehydes of intermediate No. 20 in scheme III, applicants observe that there is an ester group in intermediate No. 20. In this regard, applicants submit that since it is well known in the chemical field that the reaction favors the formation of a structurally stable 5-membered ring; thus a person skilled in the art would readily understand that hydrazine would eventuate into the ring form rather than reacting with the ester group. Moreover, in view of the specific conditions of the cyclization as described in the specification, a person skilled in the art would further expect that hydrazine would eventuate into the ring form rather than reacting with the ester group.

Specifically, the cyclization reaction is performed using buffered conditions in acetic acid which prevents a possible hydrazinolysis of the ester (see experimental details on page 35, line 25 to page 36, line 3), and this is evidenced by obtaining the claimed compounds (characterized by NMR) in good yields. Furthermore, in case of the presence of a carbonyl group in R_2, a person skilled in the art would readily understand that such carbonyl can be conveniently protected by using procedures well known in literature. Moreover, as discussed in above, the cyclization reaction is more favored with respect to the formation of the hydrazone (see for instance scheme II, intermediate 11, at page 16, lines 1-3).

Regarding the allegation that the aminolysis step would cause unwanted side reactions depending upon the R_2-NCS used, applicants submit that a person skilled in the art would readily understand this and take appropriate measures to avoid such problem.

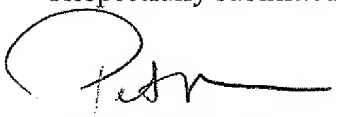
Specifically, applicants submit that the aminolysis to obtain an amide from an ester is just one of a wide array of reactions available for this purpose. As stated above for the reaction of the hydrazine, any sensitive chemical group possibly present in the remaining part of the molecule can be conveniently protected by using procedures well known in literature.

Moreover, a person skilled in the art would readily understand that the aminolysis could be achieved by an alternate means which would not affect the R_2 group. Specifically, the final amide formation could be obtained indirectly by hydrolysis of the ester (either in basic or acidic conditions) to obtain the corresponding acid to be then converted to the final amide by a variety of known synthetic procedures.

In view of the above remarks, applicants respectfully submit that the present application complies with the written description requirement. The instant rejection has been obviated, thus withdrawal of the same is respectfully requested.

Thus, in view of the foregoing amendments and remarks, it is firmly believed that the present application is in condition for allowance, which action is earnestly solicited.

Respectfully submitted,



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Enclosure: Exhibit A and Five (5) References
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